

Amendments to the Specification

Please amend the Title as follows:

**USE OF METHODS OF MANUFACTURING MEDICAMENTS COMPRISING  
FIBROBLAST GROWTH FACTOR 23 FRAGMENTS OR DERIVED OR RELATED  
POLYPEPTIDES**

Please amend Paragraph 30 as follows:

[0030] FIG. 1 is a set of polypeptide sequences and putative polypeptide sequence correlations for GPA018 (SEQ ID NO. 5), GPA019 (SEQ ID NO. 7), GPA020 (SEQ ID NO. 9), GPA022 (SEQ ID NO. 10) and GPA023 (SEQ ID NO. 13).

Please amend Paragraphs 135-136 as follows:

[00135] *Introduction and summary.* Five peptides with unidentified function were tested in mice to obtain biochemical and pharmacogenomic data that would allow a specification of their activity. Outbred CD-1 mice were treated with peptides GPA018 (SEQ ID NO. 5), GPA019 (SEQ ID NO. 7), GPA020 (SEQ ID NO. 9), GPA022 (SEQ ID NO. 10) and GPA023 (SEQ ID NO. 13) for seven days, observed for clinical signs of treatment effects (mortality, clinical signs, body weight, food consumption, haematology, clinical biochemistry) and, after sacrifice, a selected set of tissues were used for gene expression profiling. A snap freezing sampling of the tissues was performed at necropsy at the end of the treatment period. These tissues were used for mRNA expression profiling and for histopathological analysis (formalin fixation). In addition, parameters investigated in a standard exploratory study were recorded. None of the peptides had any influence on clinical or pharmacogenomic parameters. Gene expression

profiling revealed no significant changes between control and treated animals. It was concluded that the peptides were inactive and decided that no further investigations on these peptides would follow.

[00136] *Treatment.* Peptides GPA018 GPA018 (SEQ ID NO. 5), GPA019 (SEQ ID NO. 7), GPA020 (SEQ ID NO. 9), GPA022 (SEQ ID NO. 10) and GPA023 (SEQ ID NO. 13) (GeneProt, Geneva, Switzerland; see, FIG. 1) were administered subcutaneously to CD-1 mice for seven days at a dose of 300 mcg/day. The choice of CD-1 mice (an outbred strain from Charles River Laboratories, l'Arbresle, France) was made to increase the mouse organ weight and, hence, yield of RNA for microarray analysis. Four animals per treatment arm and gender were used. At the beginning of the treatment period, the animals were 12 to 14 weeks old. Body weight averaged 42.2g (38 to 45.6 g). Animals were kept under standard conditions for animal welfare.

Please amend Paragraph 157 as follows:

[00157] In the GPA018 treated kidneys of males and females combined (eight samples per group), some possible influence on genes affected by or affecting TGF $\beta$  signalling were observed (TABLE 2A and TABLE2B). GPA018 (SEQ ID NO. 5) shows some sequence similarity to the N-terminal region of mLTBP-2 (SEQ ID NO. 6) (murine latent transforming growth factor binding protein-2). LTBP proteins aid the LAP (latency associated protein)-TGF $\beta$  complex to become secreted and binds it to the ECM (extracellular matrix)-structural protein fibrillin (Annes JP *et al.*, *J. Cell Sci.* 116(Pt2):217-24 (2003); Chen S *et al.*, *Nucl. Acids Res.* 31(4):1302-10 (2003); Vehivilainen P *et al.*, *J. Biol. Chem.* 278(27):24705-13 (2003)). However, the extent of the changes after treatment was very small, usually below 1.5-fold, and similar patterns were not observed when female or male groups were investigated separately.